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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/106,172	06/26/98	TULLY	R 0/97293US

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KRASS, F	
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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/106,172	Tully
Examiner	**Group Art Unit**
Frederick Krass	1614

☒ Responsive to communication(s) filed on *Jun 26, 1998* .

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *1-11* is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1-11* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☒ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☒ None of the CERTIFIED copies of the priority documents have been

☒ received.

☐ received in Application No. (Series Code/Serial Number) _____ .

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____ .

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). *5,6*

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

Enablement Rejection

Claim 1 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for making solutions containing tamoxifen at levels of at least 1.5 g/ml comprising 10-20 percent ethanol, 10-60 weight percent glycol, and a balance of water, does not reasonably provide enablement for making solutions containing 1.5 g/ml tamoxifen in any solvent or mixture of solvents. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to the invention commensurate in scope with these claims.

Attention is directed to *In re Wands*, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:

1) the quantity of experimentation necessary,
2) the amount of direction or guidance provided,
3) the presence or absence of working examples,
4) the nature of the invention,
5) the state of the prior art,
6) the relative skill of those in the art,
7) the predictability of the art, and
8) the breadth of the claims.

The instant specification fails to provide information that would allow the skilled artisan to practice the instant invention without resorting to undue experimentation. The skilled artisan will recognize the fact that the solubilization of tamoxifen is a well known problem in the art and that, as verified by applicant's own disclosure, it is very difficult to predict the solubility of a specific

pharmaceutical salt such as tamoxifen citrate in any given solvent (see page 1, lines 25-29). Accordingly, the fact that tamoxifen citrate can be solubilized to a high degree in ethanol, glycol and water is in fact considered surprising by applicant (last two lines of page 2).

Thus, the disclosure provides no guidance as to how to reasonably predict whether other solvents or solvent mixtures, or ethanol, glycol and water in other proportions, will provide a solution comprising at least 1.5 g/ml tamoxifen. Absent a reasonable *a priori* expectation of success for a specific solvent or solvent combination producing such a solution, one skilled in the art would have to extensively test many various combinations of same to verify solubility in each case, thus requiring massive and undue further experimentation.

Indefiniteness Rejection

Claims 1-11 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

1) The term "suitable" in claim 1 is a relative term which renders the claim indefinite. The term is not defined by the claim, the specification does not provide a reasonable standard for ascertaining the requisite degree, and thus one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. Since no guidance is provided as to how "unsuitable" a given solvent can be and still fall within the scope of the instantly claimed subject matter as circumscribed by the term "suitable" the metes and bounds of the term are not clear, making it impossible to ascertain with reasonable precision when that term is infringed and when it is not.

2) Claim 7, last line, "components" lacks antecedent basis (the term should be singularized).

3) Current Markush group practice requires that one of the two general formats be used:

1) "selected from A, B or C"

or 2) "selected from the group consisting of A, B and C".

See M.P.E.P. 2173.05(h). Note that when the transitional phrase "the group consisting of" is used, the connector is "and"; when that transitional phrase is not used, the connector is "or". Thus, the phrase --- the group consisting of --- should be inserted immediately before the word "flavors" in claims 10 and 11.

Obviousness Rejection

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

1) Claim 1 is rejected under 35 U.S.C. 103(a) as being unpatentable over WO93/11757 in view of Kraus (USP 4,851,433) .

The primary reference discloses aqueous solutions of tamoxifen or its salts wherein solubility is improved by forming a cyclodextrin-drug complex. Tamoxifen is specifically used in the working examples (page 7), but tamoxifen citrate is not specified *ipsissima verba*.

The secondary reference teaches that it is well-known to provide tamoxifen in the form of its salts, including the citrate salt (column 1, lines 57-61). Exemplified compositions are ointments rather than solutions, however, as demonstrated by working example 4 (column 5, first full paragraph).

It would have been obvious to have used tamoxifen citrate in forming the cyclodextrin complexes of the primary reference given the teaching of therapeutic equivalence for tamoxifen

and its citrate salt provided by the secondary reference. It should be noted that cyclodextrin complexes are within the scope of the instant claim language and thus are not excluded thereby.

2) Claim 1 is rejected under 35 U.S.C. 103(a) as being unpatentable over WO84/01506.

The prior art discloses the use of N-methylformamide as a solvent for increasing the solubility of chemotherapeutics including tamoxifen citrate (page 5, fifth line); the reference is not anticipatory insofar as that specific agent must be selected from a list of alternative agents, but given its specific enumeration it would have plainly been obvious to do so.

Allowable Subject Matter

Claims 2-11 would be allowable if rewritten to overcome the rejection(s) under 35 U.S.C. 112, 2nd paragraph, set forth in this Office action and to include all of the limitations of the base claim and any intervening claims.

The prior art does not fairly suggest, teach or disclose applicant's solution to the technical problem of tamoxifen citrate solubilization, namely using the specific solvent combination of claim 2.

It is noted that the European Search Report has designated Derwent Abstract AN 92-033196 to be an "X" reference with regard to claims 1, 2 and 8. The reference is not available as prior art under United States practice, however, since it fails to disclose a solution having at least 1.5g/ml tamoxifen citrate, instead disclosing solutions orders of magnitude lower in concentration.

Correspondence

Any inquiry concerning the substantive issues (i.e. legal and/or technical matters relating to the determination of patentability) of this communication or earlier communications from the

examiner should be directed to Frederick Krass whose telephone number is (703) 308-4335. The examiner can normally be reached on Monday through Friday from 9:30 am to 6:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Marianne Cintins, can be reached on (703) 308-4725. The fax phone number for this Group is (703) 308-4556.

Frederick Krass
Primary Examiner
Art Unit 1614